15

20

25

References Cited

- Dahiyat, B. I., Gordon, D. B. & Mayo, S. L. (1997a). Automated design of the surface positions of protein helices. *Protein Sci* **6**(6), 1333-7.
- 5 Dahiyat, B. I. & Mayo, S. L. (1996). Protein Design Automation. *Protein Science* **5**, 895-903.
 - Dahiyat, B. I. & Mayo, S. L. (1997a). De novo protein design: fully automated sequence selection. *Science* **278**(5335), 82-7.
 - Dahiyat, B. I. & Mayo, S. L. (1997b). Probing the role of packing specificity in protein design. *Proc Natl Acad Sci U S A* **94**(19), 10172-7.
 - Dahiyat, B. I., Sarisky, C. A. & Mayo, S. L. (1997b). De novo protein design: towards fully automated sequence selection. *J Mol Biol* **273**(4), 789-96.
 - Delarue, M. & Koehl, P. (1997). The inverse protein folding problem: self consistent mean field optimization of a structure specific mutation matrix. *Pac Symp Biocomput*, 109-21.
 - Desjarlais, J. R. & Clarke, N. D. (1998). Computer search algorithms in protein modification and design. *Curr Opin Struct Biol* **8**(4), 471-5.
 - Desjarlais, J. R. & Handel, T. M. (1995). De novo design of the hydrophobic cores of proteins. *Protein Science* **4**, 2006-2018.
 - Desjarlais, J. R. & Handel, T. M. (1999). Side-chain and backbone flexibility in protein core design. *J Mol Biol* **290**(1), 305-18.
 - Desmet, J., De Maeyer, M., Hazes, B. & Lasters, I. (1992). The dead-end elimination theorem and its use in protein side-chain positioning.

 Nature 356(9), 539-542.
 - Dunbrack, R. L., Jr. & Cohen, F. E. (1997). Bayesian statistical analysis of protein side-chain rotamer preferences. *Protein Sci* **6**(8), 1661-81.
 - Eisenberg, D. & McLachlan, A. D. (1986). Solvation energy in protein folding and binding. *Nature* **319**(6050), 199-203.
- 30 Goldstein, R. F. (1994). Efficient rotamer elimination applied to protein side-chains and related spin glasses. *Biophys J* **66**(5), 1335-40.

10

15

20

- Gordon, D. B., Marshall, S. A. & Mayo, S. L. (1999). Energy functions for protein design. *Curr Opin Struct Biol* **9**(4), 509-13.
- Harbury, P. B., Tidor, B. & Kim, P. S. (1995). Repacking protein cores with backbone freedom: structure prediction for coiled coils. *Proc Natl* Acad Sci U S A 92(18), 8408-12.
- Hellinga, H. W. (1997). Rational protein design: combining theory and experiment. *Proc Natl Acad Sci U S A* **94**(19), 10015-7.
- Hellinga, H. W. & Richards, F. M. (1994). Optimal sequence selection in proteins of known structure by simulated evolution. *Proc Natl Acad Sci U S A* **91**(13), 5803-7.
- Hendsch, Z. S. & Tidor, B. (1999). Electrostatic interactions in the GCN4 leucine zipper: substantial contributions arise from intramolecular interactions enhanced on binding. *Protein Sci* **8**(7), 1381-92.
- Henikoff, S. & Henikoff, J. G. (1994). Position-based sequence weights. *J Mol Biol* **243**(4), 574-8.
- Holland, J. H. (1992). *Adaptation in natural and artificial systems*, The MIT Press, Cambridge, Mass.
- Johnson, E. C., Lazar, G. A., Desjarlais, J. R. & Handel, T. M. (1999).

 Solution structure and dynamics of a designed hydrophobic core variant of ubiquitin. *Structure Fold Des* **7**(8), 967-76.
- Jorgensen, W. L. & Tirado-Rives, J. (1988). The OPLS potential functions for proteins. Energy minimizations for crystals of cyclic peptides and crambin. *Journal of the American Chemical Society* **110**(6), 1657-1666.
- Koehl, P. & Delarue, M. (1994). Application of a self-consistent mean field theory to predict protein side-chains conformation and estimate their conformational entropy. *J Mol Biol* 239(2), 249-75.
 - Koehl, P. & Delarue, M. (1996). Mean-field minimization methods for biological macromolecules. *Curr Opin Struct Biol* **6**(2), 222-6.

25

- Kono, H. & Doi, J. (1994). Energy minimization method using automata network for sequence and side-chain conformation prediction from given backbone geometry. *Proteins* 19(3), 244-255.
- Kono, H., Nishiyama, M., Tanokura, M. & Doi, J. (1998). Designing the hydrophobic core of Thermus flavus malate dehydrogenase based on side-chain packing. *Protein Eng* 11(1), 47-52.
- Kuhlman, B. & Baker, D. (2000). Native protein sequences are close to optimal for their structures. *Proc Natl Acad Sci U S A* **97**(19), 10383-8.
- Lazar, G. A., Desjarlais, J. R. & Handel, T. M. (1997). De novo design of the hydrophobic core of ubiquitin. *Protein Sci* 6(6), 1167-78.
 - Lazar, G. A., Johnson, E. C., Desjarlais, J. R. & Handel, T. M. (1999).

 Rotamer strain as a determinant of protein structural specificity. *Protein Sci* 8(12), 2598-610.
- Lee, C. (1994). Predicting protein mutant energetics by self-consistent ensemble optimization. *J Mol Biol* **236**(3), 918-39.
 - Micheletti, C., Seno, F., Maritan, A. & Banavar, J. R. (1998). Design of proteins with hydrophobic and polar amino acids. *Proteins* **32**(1), 80-7.
- 20 Raha, K., Wollacott, A. M., Italia, M. J. & Desjarlais, J. R. (2000).
 Prediction of amino acid sequence from structure. *Protein Sci* 9(6), 1106-19.
 - Ranganathan, R., Lu, K. P., Hunter, T. & Noel, J. P. (1997). Structural and functional analysis of the mitotic rotamase Pin1 suggests substrate recognition is phosphorylation dependent. *Cell* **89**(6), 875-86.
 - Street, A. G. & Mayo, S. L. (1999). Computational protein design. Structure Fold Des **7**(5), R105-9.
 - Su, A. & Mayo, S. L. (1997). Coupling backbone flexibility and amino acid sequence selection in protein design. *Protein Sci* **6**(8), 1701-7.

- Voigt, C. A., Gordon, D. B. & Mayo, S. L. (2000). Trading accuracy for speed: A quantitative comparison of search algorithms in protein sequence design. *J Mol Biol* **299**(3), 789-803.
- Voigt, C. A., Mayo, S. L., Arnold, F. H. & Wang, Z. G. (2001).

 Computational method to reduce the search space for directed protein evolution. *Proc Natl Acad Sci U S A* **98**(7), 3778-83.
 - Weiner, S. J., Kollman, P. A., Case, D. A., Singh, U. C., Ghio, C., Alagona, G., Profeta, S. & Weiner, P. (1984). A new force field for molecular mechanical simulation of nucleic acids and proteins. *Journal of the American Chemical Society* 106(3), 765-784.